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MORGAN, LEWIS & BOCKIUS, LLP
ONE MARKET SPEAR STREET TOWER
SAN FRANCISCO, CA 94105

EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/626,096
Filing Date: July 26, 2000
Appellant(s): UMEK ET AL.

Robin Silva
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed January 7, 2009, appealing from the Office action mailed February 7, 2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

98/20162	Kayyem et al.	5-1998
5,633,134	Shuber	5-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 60-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kayyem et al. (WO 98/20162) in view of Shuber (USPN 5,633,134).

With regard to claim 60, Kayyem et al. teach a method of determining the identification of nucleotide(s) at a first detection position in a first domain of a target sequence, said target sequence comprising said first domain and a second domain, said method comprising:

a. providing an electrode with a covalently attached capture probe, wherein said capture probe has a sequence substantially complementary to said second domain of said target sequence (see p. 36 lines 10-22)

b. contacting said electrode with:

(i) said target sequence;

(ii) a first label probe substantially complementary to said first domain, comprising a first nucleotide at an interrogation position and a first electron transfer moiety (ETM) with a first redox potential (see p. 36 lines 10-22);

With regard to claim 63, Kayyem et al. teach an array of capture probes (see p. 36 lines 10-14, where the plurality of oligomers attached to a plurality of nucleic acids on a plurality of electrodes comprises the array).

With regard to claim 64, Kayyem et al. teach the first label probes contains a plurality of first ETMs (see p.36 lines 30-32).

With regard to claims 66-69, Kayyem et al. teach a ferrocene derivative (see p.41 line 21-24, where a substituted ferrocene is a ferrocene derivative and a transition metal ETM).

Kayyem et al. do not teach step (iii) a second label probe complementary to the first domain comprising a second nucleotide at said interrogation position.

More generally, Kayyem et al. do not teach using multiple ETM labeled probes for detecting the same domain. However, at the time of filing the use of multiple oligonucleotide probes specific for one domain was known and taught by Shuber. Kayeem et al. is relied on for the teaching of the use of ETMs as probes and the mechanism by which the ETMs function. Shuber is relied on for the teaching of using multiple probes to probe a single target domain. Thus, at the time of filing the use of ETMs as probes and the use of multiple oligonucleotide probes to detect specific sequences were both well known in the art. The instant claims do not set forth any new elements that were not known in the art at the time of filing, nor set forth a new use for these elements. Moreover, a review of the instant disclosure and prosecution history indicates that there are not secondary considerations when the two elements are combined that would not have been expected.

With regard to claim 61, Kayyem et al. do not teach a third label probe complementary to the first domain comprising a third nucleotide at said interrogation position.

With regard to claim 62, Kayyem et al. do not teach a fourth label probe complementary to the first target domain comprising a fourth nucleotide at said interrogation position.

Shuber teaches allele specific oligonucleotide hybridization using allele specific oligonucleotide probes.

With regard to claim 60, Shuber teaches multiple oligonucleotide probes with labels for determining nucleotides at the detection position (see abstract and col. 5 lines 13-21 and table 1, where the ASO are the labeled probes used to detect the mutations at the interrogation position)

With regard to claims 62 and 65, Shuber teach multiple probes (see col. 5 table 1, which comprises the multiple labeled probes).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection, as taught by Shuber since Kayyem states, "In general electron transfer between electron donors and acceptors does not occur at an appreciable rate when the nucleic acid is single stranded, nor does it occur appreciably unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor in the double helical structure (see p. 9 lines 21-24)." An ordinary practitioner would have been motivated to use ETM labeled oligonucleotides, as taught by Kayyem et al. with the multiple oligonucleotide probes for mutation detection because Kayyem states that no electron transfer occurs unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor. This property is particularly advantageous for the detection of nucleotide mutations using the multiple probe methods as describe by Shuber in allele specific oligonulceotide hybridization.

(10) Response to Argument

Analysis for the obviousness rejection is proper

Appellants argue the factual inquiry into the factors for obviousness is incomplete because the Office has not provided in the record any indication of the level of ordinary skill in the art. This argument is not persuasive because Graham does not require that an assessment of the level of skill be indicated in the record or in the rejection but rather requires only that an assessment is made. Additionally, as noted by Appellants the Federal Circuit provided for the level of skill ascribed to an ordinary practitioner. This skill level is not variable, therefore the level of skill ascribed to an ordinary practitioner is "one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights." This standard

is not variable and therefore no indication need be provided in the record. The only requirement made in Graham by the Federal Circuit is that the level of skill be assessed, and as required, the level of skill was assessed in making the obviousness rejection rendering the factual inquiry complete.

Differences between the prior art and the claims

Appellants argue the method of the instant claims allows for distinguishing the binding of two different label probes of different sequence in the same experiment and that in Shuber the signal from the two probes would be indistinguishable and would render the invention inoperative. This argument is not persuasive because the mechanism by which the ETMs work and are used as labels for probes is taught by Kayyem et al. Kayyem et al. do not teach using multiple ETM labeled probes for detecting the same domain. Shuber, however teaches multiple oligonucleotide probes specific for one domain. Appellants argue Shuber does not teach a second label probe comprising a second ETM with a second redox potential and that the ASO probes all have the same label. Appellants argue that Shuber teaches determining mutations by the process of elimination and a skilled artisan would not have interpreted Shuber as teaching the use of multiple different labels simultaneously. These arguments are not persuasive because Shuber is not relied on to teach a second label probe comprising a second ETM. Kayeem et al. is relied on for the teaching of ETMs and the mechanism by which the ETMs function. Shuber is relied on for the teaching of using multiple probes to probe a single target domain and Shuber does teach this. A skilled artisan would recognize that in view of the teachings of Kayeem et al. regarding ETMs and the mechanism by which the ETMs work upon reading Shuber would be motivated to use multiple probes labeled with ETMs to probe a single target domain. A skilled artisan having read the disclosure of Kayeem et al. would recognize that ETMs as labels are distinguishable one from another and having read Shuber would also recognize the advantage of using such labels on probes when probing a single domain.

Appellants argue with respect to Kayeem et al. that Kayeem et al. do not teach multiple ETM labels and that Kayeem et al. teach two ETMs the first being an electrode which does not act as a label and a second ETM which is a true label. This argument is not persuasive because as outlined above Kayeem et al. is not relied on for the teaching of a second label probe but rather Shuber is relied on for the teaching multiple probes.

Proper motivation is provided

Appellants argue that the rejection does not identify a reason that would have prompted a person of ordinary skill in the art to combine the elements in the way the invention does. This argument is not persuasive. The reason for motivation is provided for in the rejection above. Kayeem et al. teaches the properties of ETMs and specifically states that "In general electron transfer between electron donors and acceptors does not occur at an appreciable rate when the nucleic acid is single stranded, nor does it occur appreciably unless nucleotide base pairing exists in the double stranded sequence between the electron donor and acceptor in the double helical structure (see p. 9 lines 21-24)." A skilled artisan would recognize this property of electron transfer could be exploited when using an ETM as a label. Additionally a skilled artisan would recognize not only that this property is useful in a single label but in multiple label probes because it is this property, combined with the understanding that different ETMs have different redox potentials, which will allows for simultaneous probing for a single polynucleotide morphism because if there is a misalignment in the base-pairing of the double stranded probe target hybrid then electron transfer will not occur as it will if there is no misalignment.

In conclusion the combination of Kayeem et al and Shuber teach and suggest all the elements of the instant claims and there is proper motivation to combine the references. The rejections are therefore proper.

(11) Related Proceeding(s) Appendix

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Heather G. Calamita, Ph.D./
Examiner, Art Unit 1637

Conferees:

/Joseph T. Woitach/
Supervisory Patent Examiner, Art Unit 1633

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637